REMARKS

I. Amendments to the Claims:

Claims 26-34, 36-44, 46-70, 73-75, and 80-84 were pending in the instant application.

Claims 27-34, 36-40, 42-44, 46-48, 50-70, 73-75, 80, 81, and 84 were withdrawn by the Examiner as drawn to a non-elected invention.

Claims 26, 41, 49, and 82-83 are pending and under examination in this application.

Claim 26 has been amended herewith and claim 85 has been newly added. Support for the claim amendment and new claim can be found, *inter alia*, at Figures 14-19, page 8, lines 8-14; page 9, lines 14-19; the paragraph bridging pages 11-12; page 60, lines 23-31; Example 3, and Example 10. Accordingly, no new matter has been added.

Upon entry of the instant amendment to the claims, claims 26, 41, 49, 82-83, and 85 will be pending and under examination in this application.

II. Provisional Obviousness-Type Double Patenting Rejections:

Claims 26, 41, 49, and 82-83 were provisionally rejected under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1 and 6 of U.S. Appl. No. 09/965,395 (*see,* Office Action, pages 2-3).

Applicant notes that U.S. Appl. No. 09/965,395 was abandoned and therefore is not co-pending with this application. Accordingly, the grounds for this provisional rejection have been rendered moot.

Accordingly, Applicant respectfully requests that this rejection be reconsidered and withdrawn.

III. Rejections Under 35 U.S.C. § 112, First Paragraph:

Claims 26, 41, 49, and 82-83 are rejected under 35 U.S.C. § 112, first paragraph, enablement, as purportedly failing to comply with the enablement requirement (*see,* Office Action, pages 3-7).

The sole independent claim in the instant application, claim 26, as amended, is directed to a method for treating or increasing resistance to a viral infection in a patient, comprising reactivating the thymus of the patient. Applicant respectfully submits that this amended claim as well as those dependent thereon are fully enabled.

The Office Action states that the breadth of the claims encompasses preventing or treating any disease by reactivating the thymus of the patient (*see,* Office Action, page 4). In response to the three issues relating to breadth raised in the Office Action, Applicant notes that: (i) the presently amended claims are specifically directed to a viral infection; (ii) in addition, the presently amended claims are not directed to "preventing" any disease, but rather to a method for treating or increasing resistance to a viral infection; and (iii) "castration" and "chemical castration" are defined at page 34, lines 12-24 of the application as filed.

Applicant further notes that the application provides sufficient enablement for the amended claims, *inter alia*, at page 8, lines 8-14; page 9, lines 14-19; the paragraph bridging pages 11-12; page 60, lines 23-31; Example 3, Figures 14-19, and Example 10, of the application as filed. Specifically, the application teaches that reactivation of the thymus can enhance the immune response to viral infections.

For example, the application teaches that reactivation of the thymus can enhance the immune response to Herpes Simplex Virus (HSV) infection. Mice (with and without disruption of sex steroid signaling) were immunized in the footpad with HSV and the popliteal lymph node was analyzed at day 5 (D5) post-immunization. In addition, the footpad was removed and homogenized to determine the virus titer at particular time-points throughout the experiment. The regional (popliteal) lymph node response to HSV infection was examined (*see,* Figs. 14-19 of the application as filed).

A significant decrease in lymph node cellularity was observed with age (*see,* Figs. 14A, 14B, and 16 of the application). At D5 post-immunization, the mice with a disruption of sex steroid signaling were found to have a significantly larger lymph node cellularity than the aged mice (*see,* Fig. 16 of the application). Although no difference in the proportion of activated ($CD8^+CD25^+$) cells was seen with age or post-disruption of sex steroid signaling (*see,* Fig. 17A of

the application), activated cell numbers within the lymph nodes were significantly increased with disruption of sex steroid signaling when compared to the aged controls (*see*, Fig. 17B of the application). Further, activated cell numbers correlated with that found for the young adult (*see*, Fig. 17B of the application), indicating that cytotoxic T cells (CTLs) were being activated to a greater extent in the mice with a disruption of sex steroid signaling, but the young adult may have an enlarged lymph node due to B cell activation. This was confirmed with a CTL assay detecting the proportion of specific lysis occurring with age and post-disruption of sex steroid signaling (*see*, Fig. 18 of the application). Aged mice showed a significantly reduced target cell lysis at effector:target ratios of 10:1 and 3:1 compared to young adult (2-month) mice (*see*, Fig. 18 of the application). Disruption of sex steroid signaling restored the ability of mice to generate specific CTL responses post-HSV infection (*see*, Fig. 18 of the application).

In addition, while overall expression of Vβ10 by the activated cells remained constant with age (*see*, Fig. 19A of the application), a subgroup of aged (18-month) mice showed a diminution of this clonal response (*see*, Figs. 15A-C of the application). By six weeks post-disruption of sex steroid signaling, the total number of infiltrating lymph node cells and the number of activated $CD25^+CD8^+$ cells had increased to young adult levels (*see*, Figs. 16 and 17B). More importantly however, castration significantly enhanced the CTL responsiveness to HSV-infected target cells, which was greatly reduced in the aged mice (*see*, Fig. 18 of the application) and restored the CD4:CD8 ratio in the lymph nodes (*see*, Fig. 19B of the application). Indeed, a decrease in $CD4^+$ T cells in the draining lymph nodes was seen with age compared to both young adult and mice with a disruption of sex steroid signaling (*see*, Fig. 19B of the application), thus illustrating the vital need for increased production of T cells from the thymus throughout life, in order to get maximal immune responsiveness. In sum, these data show that disruption of sex steroid signaling enhanced the immune response to HSV infection.

Applicant also draws the Examiner's attention to the Declaration of Dr. Boyd that is attached with this response (*see*, **Appendix A**). This Declaration further supports the enablement of the amended claims. Specifically, the Declaration provides experimental data that shows that the claimed method is useful in the treatment of influenza infections. More

specifically, the data show that reactivation of the thymus (by sex steroid ablation) increases naive T cell output from the thymus in aged mice, which results in increased numbers of $CD8^+$ T cells responding to influenza infection, which in turn, increases overall antiviral activity and reduces viral load in the lungs.

In view of the foregoing remarks, Applicant submits that the grounds for this enablement rejection have been overcome.

Accordingly, Applicant respectfully requests that this rejection be reconsidered and withdrawn.

CONCLUSIONS

In view of the amendments and arguments provided above, Applicant respectfully requests reconsideration and withdrawal of the outstanding rejections.

Applicant petitions for a three-month extension of time to respond to the outstanding Office Action. Please charge the requisite fees to our Deposit Account No. 08-0219. No additional fees are believed to be due in connection with this correspondence; however, if any fees are due, please charge the needed fees to our Deposit Account No. 08-0219.

The Examiner is encouraged to telephone the undersigned at the telephone number given below advance prosecution of this application.

Respectfully submitted,

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